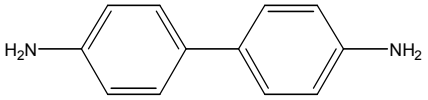
BENZIDINE
CAS No. 92-87-5
First Listed in the *First Annual Report on Carcinogens*



CARCINOGENICITY

Benzidine is *known to be a human carcinogen* based on sufficient evidence of carcinogenicity in humans (IARC V.29, 1982; IARC S.4, 1982). Case reports and follow-up studies of workers provide sufficient evidence that occupational exposure to benzidine is strongly associated with an increased risk of bladder cancer. The association is strengthened by data that suggest that the incidence of this cancer in workers decreased after a reduction in industrial exposure.

An IARC Working Group reported that there is sufficient evidence of carcinogenicity of benzidine in experimental animals (IARC V.29, 1982; IARC S.4, 1982). When administered in the diet, benzidine induced urinary bladder carcinomas in dogs and increased the incidence of benign and malignant cholangiomatous tumors and hepatocellular tumors in hamsters of both sexes. When administered by gavage, benzidine induced multiple mammary carcinomas in female rats. When administered by subcutaneous injection, benzidine induced hepatocellular carcinomas and adenomas and cholangiomas in mice of both sexes. When administered by subcutaneous injection, benzidine induced hepatomas, cystocholangiomas, or hepatocellular carcinomas, tumors of the Zymbal gland, and local sarcomas in rats of both sexes. In another study, subcutaneous injection induced mammary adenocarcinomas in female rats. When administered by intraperitoneal injection, benzidine induced a dose-related increase in the incidence of benign and malignant mammary tumors and adenomas and carcinomas of the Zymbal gland in female rats.

PROPERTIES

Benzidine occurs as a grayish-yellow, white, or reddish-gray crystalline powder. It is slightly soluble in hot water, boiling ethanol and diethyl ether. When heated to decomposition, it emits highly toxic fumes of nitrogen oxides (NO_x).

USE

Benzidine, an industrial chemical, has been used for more than 60 years as an intermediate in the production of azo dyes, sulfur dyes, fast color salts, naphthols, and other dyeing compounds. More than 250 benzidine-based dyes have been reported (IARC V.29, 1982). Benzidine-based dyes are used primarily for dyeing textiles, paper, and leather products. There are approximately 550 dye applications. Approximately 50% of the dyes are applied to textiles, 45% to paper, and 5% to leather (NCI DCCR, 1975). Other uses of benzidine include its being a reagent for hydrogen peroxide in milk, a stain in microscopy, a stiffening agent in rubber compounds, a laboratory reagent for the detection of hydrogen cyanide and sulfate, for

quantitative determination of nicotine, and as a spray reagent for sugars (HSDB, 1997). In recent years, general use of benzidine has fallen dramatically because of its potential carcinogenicity (IARC V.29, 1982).

PRODUCTION

Benzidine is no longer manufactured for commercial sale in the United States (IARC V.29, 1982; SRIa, 1986; USITC, 1988; ATSDR, 1995-K008). All large-scale production was discontinued in 1976 (HSDB, 1997). The 1998 Chemical Buyers Directory, however, does identify one U.S. supplier (Tilton, 1997). The Chem Sources International directory identified one high volume and four bulk suppliers of the ten overall listed suppliers of benzidine in 1990 and two domestic suppliers of benzidine in 1988 (Chem. Sources International, 1990, 1988). Currently, all benzidine production is for captive consumption and it must be maintained in closed systems under stringent workplace controls (ATSDR, 1995-K008). An estimated production of only 227 kg (500 lb) is given for 1983, though this may omit some captive production (ATSDR, 1995-K008). The 1979 TSCA Inventory identified one company producing 500 lb of benzidine in 1977 (TSCA, 1979). Prior to 1977, U.S. production of benzidine amounted to many millions of lb per year (IARC V.29, 1982).

In recent years, there have been no imports of benzidine, but benzidine-based dyes, such as Direct Black 38 (in the *Ninth Report on Carcinogens*), are still imported. The latest figure found was for 1980, when 8900 lb of the compound were imported into the United States (ATSDR, 1995-K008). Data on exports were not available.

EXPOSURE

The primary routes of potential human exposure to benzidine are inhalation, ingestion, and dermal contact. Benzidine may get into the respiratory tract from accidental releases into the air; into the gastrointestinal tract from contaminated fingers, cigarettes, or food; and onto the skin directly or from contaminated clothing and gloves (NCI DCCR, 1975). Before 1974, benzidine and its derivatives were manufactured and used in open systems that permitted atmospheric releases at the workplace. Under OSHA regulations adopted in 1974, only closed systems were permitted. Although atmospheric emissions were expected to be reduced because of these regulations, there were no data available that reflected current concentrations of benzidine in air (ATSDR, 1995-K008).

The major release routes of benzidine to the environment appear to be by wastewaters and sludges, and by solid wastes generated by the use of benzidine and production of benzidine-based dyes. The median concentrations of benzidine in waste effluents, ground water, surface water, and soils appear to be low probably because significant levels are associated with localized areas of contamination. The production and utilization of benzidine-based dyes has decreased in the last 30 years, and environmental and health regulations have been implemented to reduce release of benzidine to the environment (ATSDR, 1995-K008).

Although the risk of the general population from benzidine is not known, available data suggest the potential for exposure via environmental media is almost nil. For food, low levels can be found in synthetic coloring agents added to some prepared foods, which, once ingested, can be metabolized into benzidine; this, however, poses a negligible risk (ATSDR, 1995-K008).

In most cases, benzidine is a hazard only in the vicinity of dye and pigment plants where

wastes may escape or be discharged. Potential health risks exist for workers in the production of benzidine and its congeners and their conversion to azo dyes and for workers in the garment, leather, printing, paper, and homecraft industries where benzidine-based dyes are used (ATSDR, 1995-K008). The National Occupational Exposure Survey (1981-1983) indicated that 15,554 workers, including 426 women, potentially were exposed to benzidine (NIOSH, 1984). The NIOSH numbers were not based on actual measurements. Workers in the United States routinely wear protective equipment to eliminate inhalation and skin contact (ATSDR, 1995-K008). No TLV has been assigned for benzidine because it is a recognized human carcinogen (ACGIH, 1996). All exposures should be kept to an absolute minimum.

Benzidine was not reported to be discharged to air, surface water, or land from manufacturing and processing facilities in the United States from 1987 to 1992 for the Toxic Chemical Release Inventory. Since only certain types of facilities are required to report, it is possible that small quantities have been released and from other types of facilities (ATSDR, 1995-K008).

REGULATIONS

In 1980, CPSC collected economic and toxicological data to propose a ban on the use of benzidine-based dyes in direct consumer dye products. CPSC also completed studies on the dermal penetration of two benzidine congener dyes with negative results. The use of benzidine congener dyes in consumer products and commercial textile applications has been decreased voluntarily. Therefore, CPSC voted to deny the petition that requested a ban of these consumer dye products. Educational materials have been developed to warn artists of the potential hazard of these dyes.

EPA regulates benzidine under the Clean Water Act (CWA), the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA), the Resource Conservation and Recovery Act (RCRA), the Superfund Amendments and Reauthorization Act (SARA), and the Toxic Substances Control Act (TSCA). Effluent discharge guidelines have been set under CWA, and benzidine is subject to reporting rules under CWA, SARA, and TSCA. A reportable quantity (RQ) of 1 lb (0.454 kg) has been proposed for benzidine under CERCLA. It is regulated as a hazardous constituent of waste under RCRA. FDA, under the Food, Drug, and Cosmetic Act (FD&CA), also regulates the amount of benzidine in various color additives for use in food, drugs, and cosmetics. The benzidine concentration in food colorants is limited to 1 ppb, except for D&C red no. 33, which can contain up to 20 ppb benzidine. NIOSH (1994) has recommended that exposure to benzidine be the lowest feasible concentration. OSHA, which has established protective standards for occupational exposure to benzidine, regulates benzidine under the Hazard Communication Standard and as a chemical hazard in laboratories. Regulations are summarized in Volume II, Table A-9.